PRINCIPLES OF NUTRITIONAL SUPPORT FOR PATIENTS WITH RENAL DISEASE

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Nutritional management of patients with renal disease tailors dietary intake to diminished renal function while continuing to meet all nutrient requirements. Normally, the kidney has primary responsibility for maintaining the volume and composition of body fluids, and, with approximately two million nephrons, it possesses great functional reserve. During the gradual progression to renal failure, through a process known as glomerulotubular balance, water, electrolyte, and acid-base balance are maintained until 70 to 80% of renal function is lost.[1] Diet, the source of metabolic substrates including water, electrolytes and potential acid and base, must be modified during this time of advancing renal insufficiency to limit the kidney's excretory load. Another goal of diet therapy is to prevent or to correct the nutritional deficiencies that frequently accompany the progression to uremia.[2]

Currently, there are 60,000 to 70,000 dialysis patients in the United States. A recent nationwide cooperative study[3] found that even relatively healthy dialysis patients have numerous nutritional deficiencies. Assessment of nutritional status in chronic dialysis patients can be difficult. Commonly used parameters such as the creatinine-height ratio cannot be used because less than expected amounts of creatinine in the urine reflect diminished renal excretion and not a smaller muscle mass. The patient's weight as a percent of ideal body weight is often an impractical parameter due to the inexactness of determining the patient's current "dry weight." (Dry weight refers to the weight of a patient, below which significant dialysis-associated hypotension will occur.) Serum albumin and dietary diaries are as insensitive to nutritional deficiencies in these patients as in the general population. Therefore, in our dialysis unit, nutritional status is assessed using serum transferrin levels and anthropometric measurements. The anthropometric determinations used include triceps and subscapular

skinfold thickness and midarm circumference. In this way, body fat as well as lean body mass can be assessed. Regardless of the methods used, chronic dialysis patients are often found to be protein and/or fat depleted. Not only are total protein stores low, but many abnormalities in amino acid metabolism have been described.[4] In the past, chronic dialysis patients were maintained on low protein diets, but current recommendations recognize the frequency and associated morbidity of protein depletion.[5] Thus, chronic hemodialysis patients are prescribed diets containing approximately 1 g/kg/d of protein, one half of which is of high biologic value. Patients maintained with continuous ambulatory peritoneal dialysis are allowed approximately 1.3 g/kg/d. This larger intake is needed to replace the protein lost across the peritoneum during continuous ambulatory peritoneal dialysis.[6] These more liberal protein guidelines are designed to maintain chronic dialysis patients in neutral nitrogen balance without producing surfeit of byproducts of protein metabolism.

In normal individuals caloric requirements are determined in part by activity levels. And, although the activity level of stable dialysis patients is low,[7] their daily caloric requirements are great. To maintain nitrogen balance, to prevent endogenous or exogenous protein from being used for gluconeogenesis, and to increase the efficiency of protein metabolism, caloric intake should be in the range of 35 to 45 cal/kg/d.[8] The high incidence of hyperlipidemia, premature atherosclerosis, and death from atherosclerotic vascular disease in chronic dialysis patients makes the selection of the caloric sources very important. Sanfelippo et al. have shown that a diet with a caloric content of 55% fat with a polyunsaturated/saturated ratio of 2 and 35% carbohydrate can correct the hypertriglyceridemia of chronic renal failure.[9] The long-term effects of such a diet, however, remain to be determined. Recently, the relationship of secondary carnitine deficiency to hypertriglyceridemia has been examined.[10] Because the incidence of secondary carnitine deficiency is unknown and because several clinical trials have given varied results, recommendations regarding carnitine supplementation cannot be made at this time.

Recommendations for sodium, potassium, calcium, and phosphate intake can be found in several recent reviews.[11,12] Vitamin D supplementation, when used to treat hypocalcemia, should be withheld until hyperphosphatemia is first controlled. This will help prevent metastatic calcification of soft tissues and vessels. The treatment of

hyperphosphatemia with aluminum-containing antacids has raised the problem of chronic aluminum toxicity. Clinically, this takes the form of "dialysis dementia" and/or a form of osteomalacia.[13,14] Dialysis dementia is a progressive, often fatal neurologic condition in chronic hemodialysis patients. The source of aluminum is both the dialysis water and phosphate-binding antacids. While the water can and should be treated to remove excess aluminum, phosphate-binding antacids cannot be withheld at this time. These aluminum-containing binders remain essential in the therapy of hyperphosphatemia and its sequellae of secondary hyperparathyroidism and bone disease. Another disorder of mineral metabolism described in uremic and dialysis patients is chronic zinc deficiency. Zinc deficiency has been associated with abnormalities in taste and sexual function, which can be corrected with supplementation.[15] Because of potential toxicity, zinc supplements should be given only when measured plasma levels are low.

The essential role for nutritional therapy in the management of patients with end stage renal disease is well accepted. These patients, however, represent only a small percentage of the total number of patients with renal disease. The function of nutritional therapy in the management of patients with advanced renal insufficiency (serum creatinine 8 to 10 mg/dl) or early, asymptomatic renal insufficiency (serum creatinine 2 to 4 mg/dl) is less well defined, and currently is an area of active investigation and debate. For several decades it has been known that uremic patients feel better with a low protein diet. The symptoms most often improved are gastrointestinal complaints of anorexia, nausea, and vomiting. These patients, with advanced renal insufficiency, do not yet require dialysis, but are severely limited in their ability to excrete end products of metabolism. At a time when the availability of dialysis was very limited, a major advance in the dietary management of these patients occurred when Giordano[16] described the utilization of endogenous and exogenous urea in the formation of nonessential amino acids. Giovanetti and Maggiore[17] then described the use of a high caloric, low protein diet supplemented with essential amino acids. Patients on such a diet not only maintain neutral nitrogen balance and experience relief of many uremic symptoms, but also benefit from a delay in the need for dialysis. These low, approximately 20 to 25 g, protein diets are monotonous and are not very palatable to American tastes. Kopple et al. compared a 20 g to a 40 g protein diet,[18] and found that, while symptomatic improvement was

similar on both diets, only 1/17 patients adhered to the 20 g diet versus 8/13 patients on the 40 g protein diet.

Why uremic symptoms are relieved by a low protein diet is unknown. Despite years of active investigation, no single uremic toxin has been found. And while urea alone is not the uremic toxin, low protein diets do reduce levels of urea and other nitrogenous metabolites which could contribute to the syndrome of uremia. To further lower exogenous nitrogen levels, keto-analogues of amino acids were added to the diet. Keto-analogues, once transaminated in the body, can replace essential amino acids, and diets consisting of 20 to 25 g of protein supplemented with ketoacids are capable of maintaining patients in neutral nitrogen balance. A further refinement of diet therapy with essential amino acids or keto-analogues is the attempt to correct abnormal amino acid profiles.[19] While the benefits of normalized amino acid profiles in tissue and/or serum are unclear, it was noted by Walser and others that renal function could improve in patients with such a diet.[20]

The limited availability of keto-analogues and poor patient acceptance of essential amino acid preparations keeps diets based on these supplements in the realm of clinical research. In practice, patients with advanced renal insufficiency, when placed on protein restricted diets, are given 0.6 g/kg of protein. When 50% of the protein is of high biologic value, nitrogen intake can be limited but still allow enough variety to encourage patient compliance. Serum proteins and anthropometric measurements are stable for many months on such a diet, but Bonomini[21] found that patients maintained by a low protein diet fared worse once dialysis was necessary.

It has long been recognized that the level of dietary protein could affect renal function. In 1939 Smadel and Farr[22] showed that a low protein diet could ameliorate the course of nephrotoxic serum nephritis in rats. A similar beneficial effect has been shown in other experimental animal models of renal disease, and has recently been described in man.[23] While some investigators[24] attribute this effect to the phosphate restriction which accompanies protein restriction, other studies[25] found similar results while controlling phosphate levels. Brenner[26] and others have shown that dietary protein affects glomerular blood flow and resistance and that the hyperemia resulting from a protein load may lead to glomerular sclerosis. The implications of this work are considerable. Should a patient with early renal insufficiency be placed on a low protein

diet? Can an asymptomatic patient adhere to such a diet with its concomitant changes in life style? How severe should the protein restriction be, and what are the long-term effects of protein restriction? As discussed in a recent editorial,[27] it is too early to answer these questions, but the possibility of altering the course of renal disease with diet therapy is very exciting.

Renal disease is associated with numerous disorders of metabolism and nutrition. While diet therapy in patients with renal disease has traditionally been directed toward correcting these abnormalities, recent emphasis has shifted to the possibility of altering the course of the renal disease itself.

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